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EXAMINER	
LIU, SAMUEL W	

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 05/19/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/889,330	KOLTERMAN ET AL.	
	Examiner	Art Unit	
	Samuel W Liu	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 April 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-83* is/are pending in the application.

4a) Of the above claim(s) *43-83* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12/20/03 & 8/23/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the claims

Claims 1-83 are pending.

Election/restriction

Applicant's election with traverse of Group I, claims 1-42 in the response filed 2 April 2004 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 43-83 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention. Therefore, claims 1-42 are under examination to the extent that they are drawn to the elected invention.

Please note that applicant's preliminary amendment filed 13 July 2001 which adds claims 75-83 has been entered.

IDS

The references of IDS filed 20 December 2003 and IDS filed 23 August 2002 have been considered.

Specification/Claim/ Objections

The disclosure is objected to because of the following informalities:

(1) In page 2, line 26, "GLP-1" should be spelled out in full for the first instance of use; see also page 6, line 19, "ICV"; and page 60, line 27, "RP-HPLC".

(2) In page 21, line 28, "at 0 weeks" should be changed to "at 0 week".

(3) In page 22, line 11, "SEQ ID NOS 9-391" should be changed to "SEQ ID NOs: 9-391"; similarly, "page 28, line 16, "SEQ. ID. NOS." should be changed to "SEQ ID NOs:". The same change should be made throughout the specification.

(3) In page 51, line28, "1 μg - 30 μg" is suggested to be changed to "1 - 30 μg" for a consistency; see the same page line 30 where recites "1-30 μg".

(4) In page 57, line 24, "body wt." should be changed to "body weight".

(5) In page 200, line 20, the phrase "(GLP-1)" does not appears to be there; or, the phrase would introduce an ambiguity; which one was "GLP-1 [7-36]NH_2" or "GLP-1" purchased?

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter that the applicant regards as his invention.

Claims 7, 9, and 12-42 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 7 recites the limitation "said preservative". There is on antecedent basis for this limitation in claim 5 from which claim 7 depends. For examination purpose, claim 7 has been taken to being dependent from claim 6.

Claim 9 appears to be duplicate in view of claim 7 by reciting "according to claim 7, further comprising m-cresol" as claim 7 has already set forth "preservative is m-cresol". For examination purpose, claim 9 has been taken to being dependent from claim 8.

Claim 14 is unclear in "preferably mannitol" because the claim does not make it clear regarding whether or not mannitol refers to the recited "carbohydrate or "iso-osmolality modifier". Claim 14 recites "about 0.005% to about 0.4% (w/v)" wherein "0.005%" lacks unit (e.g., 0.005% (w/v)). The same are the recitations "about 0.02 to 0.5% (w/v)" and "about 1.0% to about 10% (w/v)" in claim 14; see also claim 15-16, 23, 32, 34-35 and 39.

Claim 26 is not apparent in the phrase "0.9% saline" because there is no unit associated with "0.9%". For example, sodium chloride, 0.9% (w/v) solution, i.e., isotonic saline is a solution wherein 0.9 g of sodium chloride is dissolved in total volume of 100 ml (not 100 g of final weight of the solution); thus, use of different units would result in different concentrations of sodium chloride, for instance. A unit is thus required. Additionally, claim 26 is indefinite because it is not clear if up to 0.9% of carbohydrate or polyhydric alcohol is replaced by said saline.

Claim 29 recites "bulking agent"; the recitation is unclear because the specification does not clearly define what the bulking agent is; does it refer to any bi-compatible polymer (e.g., methylcellulose) or chemical polymer or high molecular weight compounds?

Claim 30 recites the limitation "said bulking agent". There is on antecedent basis for this limitation in claim 28 from which claim 30 depends. For examination purpose, claim 30 has been taken to being dependent from claim 29.

Claim 32 recites the limitation "said bulking agent". There is on antecedent basis for this limitation in claim 29 from which claim 32 depends. For examination purpose, claim 30 has been taken to being dependent from claim 31.

Claim 33 recites the limitation "said surfactant". There is on antecedent basis for this limitation in claim 30 from which claim 33 depends. For examination purpose, claim 33 has been taken to being dependent from claim 31.

Claim 34 recites "and, wherein said exendin ..." wherein "and" appears to be misplaced which renders the claim indefinite. Also, claim 34 is indefinite in the recitation "less than about 100% (w/w)" because "less than" is open-ended towards zero, i.e., the recitation refers to an undetermined or undefined range of the claimed exendin amount; does the recitation includes 0% (w/v)? The dependent claims are also rejected.

Claim 35 recites "about 0% to about 99% (w/v)" wherein "0%" renders the claim indefinite because it is unclear reading whether or not 0% points to none of carbohydrate or polyhydric alcohol being a component of the claimed bulking agent.

Claim 30 recites the limitation "said bulking agent". There is on antecedent basis for this limitation in claim 28 from which claim 30 depends. For examination purpose, claim 30 has been taken to being dependent from claim 29.

Claim 37 recites "bulking agent" which has been already recited in claim 34 from which claim 37 depends. Clarification of this is required.

Claim 39 recites the limitation "said surfactant". There is on antecedent basis for this limitation in claim 37 from which claim 39 depends. For examination purpose, claim 39 has been taken to being dependent from claim 38.

Claim Rejections - 35 USC §103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-5, 8, 10-22 and 28-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hiles, R. A. et al. (US Pat. No. 6506724).

Hiles et al. teach a pharmaceutical formulation suitable for parental administration comprising (i) exendin or exendin agonist (see abstract and col. 14, lines 39-58); (ii) a buffer; and (iii) an iso-osmolality (i.e., isotonicity) modifier, e.g., mannitol (see col. 15, lines 16-19), which is applied to the instant claim 1.

Hiles et al. teach said buffer is acetate/acetic acid buffer (see col. 15, line 10), as applied to the instant claim 2.

Hiles et al. teach said isotonicity modifier is mannitol (see col. 15, line 19), as applied to the instant claim 3.

Hiles et al. teach said buffer solution has pH from about 3.0 to 8.0, preferably a pH from about 3.5 to 5.0 (see col. 15, lines 3-5), which is applied to the instant claims 4-5, 8 and 10-11.

Hiles et al. teach the above said formulation is prepared in a liquid solution (see col. 15, lines 62-67), as applied to the instant claims 12 and 28.

Hiles et al. also teach the above said formulation can be prepared in a solid dosage forms, i.e., dry powder (see col. 16, lines 50-54), as applied to the instant claim 13.

Hiles et al. teach exendin-4 in the claimed formulation is about 0.1% (w/v). The calculation for this is the following. At column 80, lines 18-19, Hiles et al. teach the exendin-4 being administered is about 232.16 nM (see col. 80, lines 20-21); as exendin-4 has molecular weight of ~ 4,736 daltons (see column 6, lines 19-23, where indicates exendin-4 peptide consists of 39 amino acids of SEQ ID NO:2); then, 232.16 nM gives rise to 0.1 mg/100 ml, i.e., 0.1% (w/v). Note that claim 14, as written, sets froth that the claimed formulation comprises the exendin in an aqueous system, which is a buffer (acetate, or citrate, or phosphate, or glutamate buffer), or about 1.0%-10% (w/v) of carbohydrate, or polyhydric alcohol, or iso-osmolality modifier; the pH of the aqueous system is about 3.0 –7.0. Because, as stated above, Hiles et al. has taught the pharmaceutical formulation suitable for parental administration comprising (i) exendin or exendin agonist (see abstract and col. 14, lines 39-58); (ii) acetate buffer with pH value of about 3.0 to 8.0 (see col. 15, lines 2-11), and/or (iii) an iso-osmolality modifier, e.g., mannitol (see col. 15, lines 16-19), and because Hiles et al. teach exendin in the administrated formulation is about 0.1% (w/v) (see the above statement), the Hiles' teachings are applied to the instant claim 14.

Since Hiles et al. also teach the administrated exendin (in the formulation) is about 16.47 nM (see col. 80, line 12), which is calculated to be equivalent to about 0.007% (w/v) (see the above for the calculation), the above Hiles et al. teachings meet the limitation set forth in the instant claims 15-16.

Hiles et al. teach the pharmaceutical formulation may comprise polyethylene glycol which is a polyhydric alcohol compound (Note that polyhydric alcohol is also known as polyol that includes polyethylene glycol) in order to facilitate administration (see col. 15, lines 52-58), as applied to the instant claim 17.

Hiles et al. teach the formulation may comprise mannitol (see col. 15, line 19), as applied to the instant claim 18.

Also, Hiles et al. teach the formulation may comprise a carbohydrate, e.g., lactose for facilitating administration (see col. 15, lines 52-55), as applied to the instant claim 19.

Hiles et al. teach the formulation solution is isotonic comprising isotonic modifier, e.g., mannitol (see col. 15, lines 16-21), as applied to the instant claim 20.

Since Hiles et al. teach that the preferable pH of the above said solution is about 3.5 to 5.0 (see col. 15, lines 2-5), as applied to the instant claims 21-22.

Hiles et al. teach the above said formulation which is solid dosage form further comprises a bulking agent, e.g., isotonicity modifier such as mannitol (see col. 15, lines 18-19), which anticipates the instant claims 29-30.

Further, Hiles et al. teach the above said formulation further comprises a surfactant, e.g., non-ionic detergent (see col. 15, line 65 to col. 16, line 2), as applied to the instant claim 31.

Although the above Hiles et al. teachings as to formulating exendin in the pharmaceutical composition are not presented in the working examples 1-186, it would have been obvious to a person having ordinary skill in the art to prepare the said pharmaceutical composition because Hiles extensively teach that administering exendin for treating condition, e.g., reducing blood glucose (see the patent claims 1-10), and because the administering exendin inevitably requires formulating exendin in the pharmaceutical composition; and indeed, Hiles et al. teach such the pharmaceutical composition (see the above statement). Thus, the skilled artisan would have readily formulated exendin in the pharmaceutical composition according to the above Hiles et al. teachings, and therefore, successfully arrive at the claimed invention. Therefore, the claimed invention was *prima facie* obvious to make and use the invention at the time it was made.

The claims 1-2, 6, 12-13 and 28-31 are rejected under 35 U.S.C 103(a) as being unpatentable over Larsen, B. D. et al. (US Pat. No. 6528486).

Larsen et al. teach a pharmaceutical formulation suitable for parental administration comprising (i) exendin (see col. 13, lines 41-45); (ii) a buffer (see col. 14,line 8); and (iii) sucrose that is an iso-osmolality modifier (see col. 14, line 3), which is applied to the instant claim 1.

Larsen et al. teach said buffer is an acetate buffer (see col. 14, lines 53-59), as applied to the instant claim 2.

Larsen et al. teach the above said formulation further comprises a preservative (see col. 14, line 37), as applied to the instant claim 6.

Larsen et al. teach the above said formulation is prepared in a liquid composition for administration (see col. 13, lines 61-62), as applied to the instant claims 12 and 28.

Larsen et al. also teach the above said formulation is lyophilized for administration (see col. 14, lines 44-47), as applied to the instant claim 13.

Larsen et al. teach the above said formulation is prepared as a multi-dose form (see col. 36, line 1), and teach the formulation may contain a solubilizing (bulking) agent, e.g., polyethylene glycol (see col. 14, lines 30-35), which is applied to the instant claim 29.

Since low molecular weight polyethylene glycol is an iso-osmolality agent, the above Larsen' teaching is applied to the instant claim 30.

Also, Larsen et al. teach the formulation further comprises a surfactant (see col. 14, line 35), which is applied to the instant claim 31.

Although the above Larson et al. do not examplify formulating exendin in the pharmaceutical composition or disclose the pharmaceutical composition comprising exendin in the patent claims, it would have been obvious to a person having ordinary skill in the art to prepare the said pharmaceutical composition because Larson et al. extensively teach how to administer exendin (see columns 39-46) for treating condition, e.g., treatment of excess levels of blood glucose (see the abstract), and because the administering exendin inevitably requires formulation of exendin in the pharmaceutical composition; and indeed; Larson et al. teach such the pharmaceutical composition (see the above statement). Thus, the skilled artisan would have readily formulated exendin in the pharmaceutical composition according to the above Larson et al. teachings, and thus, successfully arrive at the claimed invention. Therefore, the claimed invention was *prima facie* obvious to make and use the invention at the time it was made.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Samuel Wei Liu whose telephone number is 571-272-0949. The examiner can normally be reached from 9:00 a.m. to 5:00 p.m. on weekdays. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Christopher Low, can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 703 308-4242 or 703 872-9306 (official) or 703 872-9307 (after final). Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703 305-4700.

Samuel Wei Liu, Ph.D.

Art Unit 1653, Examiner

May 5, 2004

KAREN COCHRANE CARLSON, PH.D
PRIMARY EXAMINER